ORIGINAL

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

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LANDIS INTERNATIONAL
R & D MANAGEMENT

April 24, 2013

VIA FEDERAL EXPRESS

United States Environmental Protection Agency - East
ATTN: TSCA Section 8(e)
Room 6428
1201 Constitution Avenue, NW
Washington, DC 20004-3302

SUBJECT: Notice in Accordance with TSCA Section 8(e): Results of a Preliminary Toxicity Study of EXP-8007 in Dogs

Dear Sir/Madam:

LANDIS INTERNATIONAL, INC. (hereinafter LANDIS), Consultant and Regulatory Agent herein submits on behalf of MITSUI CHEMICALS AGRO, INC., EPA Company Number 86203, data which we believe to be reportable under TSCA 8(e). The information concerns results of a non-GLP and non-guideline preliminary study of EXP-8007 on the cardiovascular system in dogs.

The purpose of this study was to investigate the effects of EXP-8007 on the cardiovascular system.

EXP-8007 is *N*-[2-bromo-6-trifluoromethyl-4-(perfluoropropane-2-yl-phenyl]-2-fluoro-3-(*N*-methylbenzamide)benzamide.

In order to investigate the effects of EXP-8007 on the cardiovascular system, a non-GLP non-guideline preliminary study was carried out using the telemetry system in dogs.
In oral administration, doses of 30, 100, 300, and 1000 mg/kg EXP-8007 filled into gelatin capsules were cumulatively given with the interval of 3 or 4 days to the male and the female dog. Similarly, in intravenous administration, doses of 0.2, 0.6, 2, 6, and 20 mg/kg EXP-8007 dissolved in DMSO:PEG 400 (1:9) were cumulatively given with the interval of 3 or 4 days to the male and the female dog. Before dosing, dogs were surgically operated for implanting the telemetry transmitter connecting with the catheter to an abdominal aorta for monitoring of blood pressure and with 2 electrodes for electrocardiogram measurement under the pentobarbital anesthesia.

In oral administration, cumulative dosing of 30, 100, 300, and 1000 mg/kg of EXP-8007 did not influence any parameters of the electrocardiogram (PR, QT, QTc or QRS intervals), blood pressure (systolic, diastolic and average blood pressure), cardiac rate, and breathing rate.

In intravenous administration, cumulative dosing of 0.2, 0.6, 2, and 6 mg/kg did not cause any significant changes in the electrocardiogram, blood pressure, cardiac rate, and breathing rate.

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However, after intravenous dosing of 20 mg/kg, one male died due to a significant fall in blood pressure. Also, after intravenous dosing of 20 mg/kg one female exhibited a significant decrease in systolic blood pressure (123 mmHg) within 30 minutes and then increases in cardiac and breathing rates 3 hours after dosing. The systolic blood pressure for the female dog 30 minutes after dosing 0.2, 0.6, 2, and 6 mg/kg including the control was in the range of 130-144 mmHg.

LANDIS understands that reporting of results from this study under TSCA 8(e) is in accordance with EPA's policy.

Please feel free to contact Crystal Layton at (229) 247-6472 or clayton@landisintl.com if any questions arise or further information is required.

Sincerely,

Crystal Layton
Regulatory Agent for
MITSUI CHEMICALS AGRO, INC.

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